

We Claim:

*Sub. a2*

1. A modified gp120 polypeptide comprising portions of at least two conserved regions of an envelope protein selected from a primate lentivirus, wherein at least two of the glycosylation sites proximal to the CD4 binding site or chemokine receptor binding site have been altered, wherein the alteration prevents glycosylation at said sites, and wherein the modified polypeptide maintains the overall 3-dimensional structure of a discontinuous conserved epitope of the wild-type gp120.

2. The modified gp120 polypeptide of claim 1, wherein the discontinuous conserved epitope is a CD4bs epitope or a CD4i epitope.

3. The modified gp120 polypeptide of claim 2, wherein the gp120 protein is selected from the group consisting of HIV-1, HIV-2 and SIV.

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4. ~~The modified gp120 polypeptide of claim 3, wherein the gp120 protein is HIV-1.~~

5. The modified gp120 polypeptide, wherein the glycosylation sites are selected from the group of amino acids that correspond to positions 197, 276, 301 and 386 of HIV-1 strain HXBc2.

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6. The modified gp120 polypeptide of claim 2, wherein the gp120 polypeptide further contains at least one of the following changes relative to the wild-type to gp120 protein:

- (a) introduction of disulfide bonds;
- (b) filling a cavity of the gp120 protein with hydrophobic amino acid residues;
- (c) introducing a Pro residue at a defined turn structure; or
- (d) increasing the hydrophobicity across the interface between the gp120 domains.

7. A modified gp120 polypeptide comprising portions of at least two conserved regions of an envelope protein selected from a primate lentivirus wherein glycosylation sites distal to the CD4 binding site or chemokine receptor binding site have been derivatized with a molecular adjuvant, and wherein the modified polypeptide maintains the overall 3-dimensional structure of a discontinuous conserved epitope of the wild-type gp120.

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8. The modified gp120 polypeptide of claim 7, wherein the molecular adjuvant is C3d.

9. The modified gp120 polypeptide of claim 8, wherein the discontinuous conserved epitope is a CD4bs epitope or a CD4i epitope.

10. The modified gp120 polypeptide of claim 8, wherein the gp120 protein is selected from the group, consisting of HIV-1, HIV-2 and SIV.

11. The modified gp120 polypeptide of claim 10, wherein the gp120 protein is HIV-1.

12. The modified gp120 polypeptide of claim 9 or 11, wherein at least two glycosylation sites proximal to the CD4 binding site or chemokine receptor binding sites have been altered, wherein the alteration prevents glycosylation at said sites.

13. The modified gp120 polypeptide of claim 12 wherein the sites proximal to the CD4 binding site or chemokine receptor binding site are selected from the group of residues corresponding to amino acid residues 197, 276, 301 and 386 of HXBc2.

14. The modified gp120 polypeptide of claim 1, 4, 5 or 6, wherein the polypeptide further contains at least one pan-reactive T-cell helper epitopes.

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